EXHIBIT K

Abstract #12044

A priori filtering of post-operative circulating tumor DNA predicts recurrence in post- metastasectomy colorectal cancer patients without knowledge of tumor genotype

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Introduction

- ctDNA in post-operative colorectal cancer (CRC) patients correlates with molecular residual disease and may be useful for prognostication and to guide adjuvant therapy decision making.[1,2]
- We previously demonstrated that post-operative ctDNA is strongly associated with disease recurrence in patients with metastatic CRC undergoing curative intent surgery (p=0.004).[3]
- Initial studies employed clinically impractical assays indexed to individual patient specific tumor tissue-derived mutations or were confounded by non-tumor-associated somatic alterations, including variants related to clonal hematopoiesis[1].
- We previously demonstrated that using a highly sensitive CRC next-generation sequencing (NGS) panel, the detection of post-operative ctDNA does not require foreknowledge of known somatic alterations.[3]
- We developed a variant classifier to expand on this ctDNA only approach and to further differentiate tumor-derived alterations from non-tumor derived alterations with the goal of increasing specificity of ctDNA detection in post-operative CRC patients.

Methods

- CRC patients planned for hepatic metastasectomy were prospectively enrolled in an IRB approved trial (LAB10-0982).
- Pre-operative and post-operative plasma was sequenced to high depth using a 23-gene NGS panel with 96% theoretical sensitivity for CRC.[3]
- 51 metastatic colorectal cancer patients with both pre and post ctDNA results were recruited at a single institution (**Tables 1,2**). Tumor tissue was sequenced using this panel or local testing.
- ctDNA profiles from 4000 CRC pts (Guardant Health, Redwood City, CA) were used to train a variant classifier to exclude non-tumor derived alterations.
- The variant classifier was designed to identify cfDNA mutations that originate from the tumor, differentiating them from non-tumor derived mutations.

Table 1: Cohort demographics

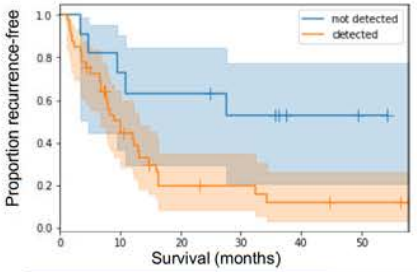
Number of unique patients	51
Median age at diagnosis (range)	55 years (33-76)
Gender	60.8% Male 39.2% Female
Histological Grade	98% Moderately Differentiated 2% Poorly Differentiated
Primary site	21.6% Right-sided 78.4% Left-sided
Presentation	15.7% Metachronous 84.3% Synchronous

Table 2: Cohort clinical features

Neoadjuvant chemotherapy	80.4%
Median number of resected tumors	2
Lymph node positive primary	66.7%
KRAS mutation positive	43%
Median time surgery to post-operative sample (range)	18 days (13-123 days)
Median follow-up (range)	42.7 months (4.4 – 59.4 months)
Recurrence	72.5% (37 patients)
Median Time to Recurrence (range)	7.8 months (1.2 – 34.5 months)

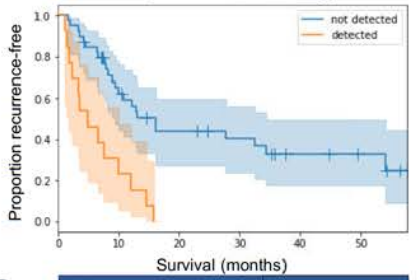
Results

No Filter



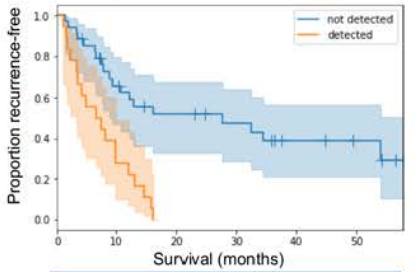
Performance Metric	No Filter
Sensitivity (pre-operative)	84.3% (43 / 51)
Sensitivity for recurrence	86.1% (31 / 36)
Specificity for recurrence	60% (9 / 15)
Recurrence Positive Predictive Value (PPV)	77.5% (31 / 40)
Recurrence Negative Predictive Value (NPV)	54% (6 / 11)

Tissue Filtering



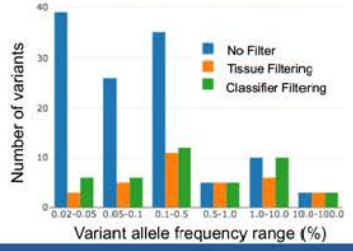
Performance Metric	Tissue Filtering
Sensitivity (pre-operative)	80.5% (33 / 41)
Sensitivity for recurrence	45.2% (14 / 31)
Specificity for recurrence	100% (10 / 10)
Recurrence PPV	100% (14 / 14)
Recurrence NPV	37% (10 / 27)

Classifier Filtering



Performance Metric	Classifier Filtering
Sensitivity (pre-operative)	82% (42 / 51)
Sensitivity for recurrence	50% (18 / 36)
Specificity for recurrence	100% (15 / 15)
Recurrence PPV	100% (18 / 18)
Recurrence NPV	45% (15 / 33)

Variant Allele Frequency distribution



Conclusions

- Recurrence prediction using post-operative somatic variant detection alone is fraught by a high clinical false positive rate.
- Many non-tumor derived mutations occur at low variant allele frequencies. However, relying solely on an allele frequency threshold to differentiate between tumor derived and non-tumor derived mutations would exclude many clinically relevant mutations.
- Filtering using tumor tissue is effective but may be clinically impractical due to added complexity and cost.
- Filtering using a novel variant classifier, without foreknowledge of tumor genotype eliminated false positives while maintaining clinically acceptable sensitivity.
- *A priori* variant classification may enable clinically feasible ctDNA diagnostics for adjuvant decision making in early-stage disease.

References

1. Tie J., et al. (2016). Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. *Sci Transl Med* 8(346)
2. Diehl, F., et al. (2008). Circulating mutant DNA to assess tumor dynamics. *Nat Med* 14(9)
3. Overman, et al. (2017). Circulating tumor DNA (ctDNA) utilizing a high-sensitivity panel to detect minimal residual disease post liver hepatectomy and predict disease recurrence. *JCO* 35(suppl).